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UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

EASTERN DIVISION

UNITED STATES OF AMERICA,

Plaintiff,

v.

CALIFORNIA STEM CELL TREATMENT CENTER, INC., a California corporation, CELL SURGICAL NETWORK CORPORATION, a California corporation, and ELLIOT B. LANDER, M.D., MARK BERMAN, M.D., individuals,

Defendants.

CASE NO. 5:18-CV-01005-JGB-KK

Hon. Jesus G. Bernal
Riverside, Courtroom 1

[PROPOSED] FINDINGS OF FACT AND CONCLUSIONS OF LAW (LOCAL RULE 52)

Action Filed:	May 9, 2018
Trial Date:	May 4, 2021
Closing Agmt.:	July 9, 2021

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FINDINGS OF FACT

I. THE SVF SURGICAL PROCEDURE IS A SURGICAL PROCEDURE THAT REMOVES AND RETURNS THE SAME HCT/PS

1. In Defendants' surgical procedure, a licensed physician targets stromal vascular fraction cells ("SVF Cells") for extraction and then implants those same cells that were removed back into the same patient during the same procedure ("SVF Surgical Procedure"). (5/12/21 PM Tr. 47:7-11 (Lander)).

2. SVF Cells are comprised of multiple cell types found within adipose tissue; these include mesenchymal stem cells ("MSC Cells"), hematopoietic cells, early (progenitors) and mature lineage stages of endothelia, pericyte progenitor cells (also called perivascular cells), red blood cells, white blood cells, lymphocytes, and fibroblasts among other cells. (5/7/21 PM Tr. 28:18-31:8 (Yong); 5/12/21 PM Tr. 46:23-47:3 (Lander)). SVF Cells are the naturally occurring part of the adipose tissue that does not contain the adipocytes (fat cells). (5/7/21 PM Tr. 28:18-31:8 (Yong); 5/11/21 AM Tr. 112:20-24 (Berman); 5/12/21 PM Tr. 47:4-6 (Lander)).

3. Cells are the smallest and most basic functional structural units in the human body. No person or device can remove a stem cell from adipose tissue without also removing other tissue. (5/7/21 PM Tr. 19:9-12 (Yong); 5/11/21 AM Tr. 112:13-19 (Berman)).

4. Surgeons routinely work on both tissues and cells that make up tissues. Surgery universally involves dissection (cutting and separation) of tissues through mechanical or chemical means, and has evolved to where surgeons can isolate cells following removal from a patient's body. (5/12/21 PM Tr. 73:20-74:1 (Lander)). Dissected tissues and cells that have been isolated can be surgically relocated and re-purposed to other parts of a patient's body. (5/12/21 PM Tr. 86:17-88:13 (Lander)).

5. Surgery is intended for the treatment and prevention of disease in the human body. (5/6/21 AM Tr. 65:12-22 (Lapteva); 5/12/21 PM Tr. 48:16-21 (Lander)).

6. Surgery can treat chronic and systemic conditions. (5/6/21 AM Tr. 65:8-12 (Lapteva)).

7. Surgery is intended to affect the structure or function of the human body. (5/6/21 AM Tr. 65:25-66:4 (Lapteva)).

8. There are no FDA-approved or disapproved surgical procedures. (5/4/21 AM Tr. 57:1-6 (Joneckis); 5/11/21 PM Tr. 14:23-15:3 (Berman)).

A. <u>The SVF Surgical Procedure Involves Surgical Removal of HCT/Ps</u>

9. SVF Cells are HCT/Ps.[1] (5/7/21 PM Tr. 19:17-20:3 (Yong)).

10. The SVF Surgical Procedure targets for removal mesenchymal stem cells and the hemopoietic or angiogenic stem cells located within the adipose tissue, not the adipose tissue itself. (5/11/21 PM Tr. 77:13-17 (Berman); 5/12/21 PM Tr. 46:13-18 (Lander)).

11. The SVF Surgical Procedure involves collecting the patient's SVF Cells naturally contained in the patient's adipose tissue and relocating those SVF Cells back into the same patient. (5/11/21 PM Tr. 77:18-21 (Berman)). The SVF Cells are already in circulation within the body. (5/11/21 PM Tr. 77:22-24 (Berman)). The SVF Surgical Procedure increases the number of available SVF Cells in circulation or around an injured area. (5/11/21 PM Tr. 48:13-15 (Berman)).

[1] HCT/Ps "means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." 21 C.F.R. § 1271.3(d).

12. The entire SVF Surgical Procedure, including the extraction, isolation, and reimplantation of SVF Cells occurs in California during a single, outpatient procedure at a surgical clinic. (5/11/21 PM Tr. 5:6-8, 57:1-10 (Berman)).

13. During the SVF Surgical Procedure, a licensed physician collects the patient's SVF Cells using a technique called "mini-liposuction via subdermal local anesthesia," which permits the liposuction of the SVF Cells, along with the adipose and connective tissue that contains the SVF Cells, under local anesthesia. (Ex. 453; 5/11/21 PM Tr. 5:6-15 (Berman)). Many cells are mechanically separated ("mechanical cutting") from the adipose tissue during the liposuction procedure, as is common in all surgeries. (5/11/21 PM Tr. 6:19-22 (Berman); 5/12/21 PM Tr. 72:24-73:15 (Lander)).

14. Next, the removed adipose tissue is centrifuged to remove the anesthesia and further mechanically dissociate the SVF Cells from the adipose tissue. (Ex. 453; 5/11/21 PM Tr. 7:12-19 (Berman)).

15. The physician then uses surgical tools—namely, Liberase enzymes and a centrifuge device—to isolate the SVF Cells from adipocytes (fat cells). (Ex. 453; 5/11/21 PM Tr. 9:4-11 (Berman)).

16. The GMP-grade Liberase was specifically developed by Roche Laboratories ("Roche") in July 2010 for use in the SVF Surgical Procedure. Roche developed a safe, GMP-grade Liberase to avoid any contamination of the SVF Cells during the SVF Surgical Procedure. (5/11/21 AM Tr. 110:19-111:1 (Berman); 5/12/21 PM Tr. 60:11-18 (Lander)). Roche entered into a private label agreement with Drs. Berman and Lander to provide the GMP-grade Liberase under the trade-name CSN-TMAX. (5/11/21 AM Tr. 111:2-6 (Berman); 5/11/21 PM Tr. 17:10-12 (Berman)).

17. All of the materials used to isolate SVF Cells during the SVF Surgical Procedure are FDA-approved drugs or FDA-cleared devices. (Exs. 384, 385 (clearance for Lipokit); 386 (clearance for Celltibator); 387, 388, 389, 390

(approval for dextrose lactated ringers solution); 391, 392, 393, 394 (approval for saline); 395, 396, 410 (proof of GMP-grade Liberase); 5/11/21 PM Tr. 13:10-15) (Berman)).

18. Further, Drs. Berman and Lander have collected an abundance of data under Institutional Review Board ("IRB")-approved protocols. (Exs. 15, 36, 48, 78, 79, 80, 81, 154, 161; 5/12/21 PM Tr. 63:1-7, 63:22-66:1 (Lander); 5/11/21 PM Tr. 36:18-25 (Berman)). The International Cell Surgical Society ("ICSS") IRB currently oversees Drs. Berman and Lander's investigational protocols. (5/11/21 PM Tr. 35:18-20 (Berman)). Drs. Berman and Lander do not sit on the ICSS IRB or have any control whatsoever over the ICSS IRB. Drs. Berman and Lander founded ICSS and only control ICSS's educational resources relating to regenerative medicine. (5/11/21 PM Tr. 35:22-36:14 (Berman); 5/12/21 PM Tr. 54:1-14 (Lander)).

19. Liberase chemically separates the SVF Cells from the extracellular matrix, and has been used for more than ten years with thousands of patients. (5/11/21 PM Tr. 9:12-10:6 (Berman)).

20. Liberase is then washed out using dextrose lactated ringers solution and centrifugation. (Ex. 453; 5/11/21 PM Tr. 10:20-11:4 (Berman)).[2] The SVF Cells are concentrated during the "washing" steps. (5/7/21 PM Tr. 63:3-25; 65:7-9 (Yong); 5/12/21 PM Tr. 76:5-19 (Lander); 5/11/21 PM Tr. 11:7-15 (Berman)).

21. Finally, the SVF Cells are filtered through a hundred micron filter and viewed through a special micrograph to ensure that the SVF Cells are free-floating, round, and do not contain "clumps of particles or debris." (5/11/21 PM Tr. 11:23-12:7 (Berman)).

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[2] Dextrose lactated ringers solution is a benign crystalloid often used during surgery. (5/12/21 PM Tr. 77:23-78:8 (Lander)).

22. The SVF Cells are then suspended in a sterile saline solution, after which they are relocated back into the patient's body. Saline is a benign crystalloid, widely used in the practice of medicine. (5/12/21 AM Tr. 56:14-19 (Berman); 5/12/21 PM Tr. 79:7-18 (Lander)). No new product is created by the use of saline as a delivery mechanism. (5/12/21 AM Tr. 56:20-22 (Berman); 5/12/21 AM Tr. 99:15-23 (Reid)).

B. The HCT/Ps That Are Removed From The Patient Are The Same HCT/Ps That Are Implanted

23. The SVF Cells are not altered, chemically or biologically, at any point during the SVF Surgical Procedure, as confirmed by Dr. Lola Reid based on her forty-five years of stem cell research and Drs. Berman and Lander's specific testing of the SVF Cells. (5/12/21 AM Tr. 99:24-100:19 (Reid)). There are no genes added to or removed from the SVF Cells during the SVF Surgical Procedure. (5/12/21 AM Tr. 100:20-23 (Reid)). The size of the SVF Cells do not change. (5/12/21 AM Tr. 101:1-2 (Reid)). The genetic makeup of the SVF Cells do not change. (5/12/21 AM Tr. 101:3-5 (Reid)).

24. The biological characteristics of the SVF Cells do not change during the SVF Surgical Procedure, including their ability to proliferate. (5/12/21 AM Tr. 101:6-8 (Reid); 5/12/21 PM Tr. 85:12-18 (Lander)). The re-implanted SVF Cells retain all their functions, including regenerative tissue repair, healing, and anti-inflammatory properties. (5/12/21 AM Tr. 85:7-86:8; 89:21-91:1, 101:9-13 (Reid)).

25. There are several methods to determine whether the SVF Cells have been physically changed during the SVF Surgical Procedure, including cell surface marker expression analysis, gene expression analysis, and proteomic analysis. (5/7/21 PM Tr. 15:9-17 (Yong)).

26. Drs. Berman and Lander, in conjunction with numerous other physicians and scientists, have tested the SVF Cells and determined that the SVF

Cells have not been altered in any way that would change them from their naturally occurring state (*i.e.*, they have the same DNA, same cell type, same flow cytometry markers). (5/12/21 PM Tr. 88:18-89:8 (Lander)). These tests and analysis have been published in peer reviewed journals. (5/12/21 PM Tr. 89:10-90:1 (Lander)).

27. Drs. Berman and Lander confirmed via flow cytometry that the SVF Cells retain their natural cell markers after they are isolated. (5/12/21 PM Tr. 88:18-89:18 (Lander)). The SVF Cells isolated during the SVF Surgical Procedure have the capacity to grow in adherent culture, meaning that they retain their inherent biological characteristics. (5/6/21 PM Tr. 13:17-14:14 (Lapteva)).

28. Indeed, the SVF Cells all displayed moderate to strong positivity for cell surface markers. (5/7/21 PM Tr. 56:6-24 (discussing cell surface markers for at least two types of SVF Cells); *id.* 60:3-61:2 (discussing cell surface markers for at least four types of SVF Cells) (Yong)).

29. The SVF Cells all demonstrated "their multipotency by differentiating into cell types such as osteoblasts, adipocytes, bone, cartilage, and muscle cells." (5/7/21 PM Tr. 61:3-17 (Yong); 5/12/21 AM Tr. 92:21-93:4 (Reid)).

30. The Liberase used to separate the SVF Cells does not break down, damage, or in any way alter the phenotypic traits and biological properties of the SVF Cells. (5/12/21 AM Tr. 79:9-80:1; 93:10-94:2 (Reid); 5/12/21 PM Tr. 76:1-4; 88:23-89:8 (Lander)). Liberase has no impact on the viability of the SVF Cells, yield of cells, and, most significantly, has no effect on the phenotype (identifying cell markers), the ability of the SVF Cells to differentiate, to proliferate, or to function in their intended capacity. (5/7/21 PM Tr. 35:7-24; 35:18-37:4; 37:5-19; 56:25-57:10 (Yong); 5/12/21 AM Tr. 79:9-80:1; 80:21-24 (Reid)). Liberase does not affect SVF Cells' ability to differentiate, the cell surface marker expression was similar, and cell viability was not significantly different. (5/7/21 PM Tr. 54:17-24; 55:15-56:2 (Yong); 5/12/21 PM Tr. 89:5-8 (Lander)).

31. Liberase does not cross or destroy the surface of the SVF Cells. Rather, Liberase enzymatically digests the extracellular matrix (*i.e.*, the collagen binding the cells together). (5/12/21 AM Tr. 80:5-19 (Reid); 5/12/21 PM Tr. 84:21-85:5 (Lander)).

32. Liberase's only effect is to allow the SVF Cells to move from one natural state (quiescent) to another natural state (regenerative), which regularly occurs in the human body. (5/12/21 AM Tr. 79:9-80:1; 89:21-91:1 (Reid)).

C. <u>There Is No Evidence That The SVF Cells Are Modified Or Altered In Any Way During The SVF Surgical Procedure</u>

33. Despite the ability to do so, the FDA has never tested a single SVF Cell at issue. (5/6/21 AM Tr. 67:13-15; 67:25-68:2 (Lapteva); 5/7/21 PM Tr. 21:11-13; 22:3-16 (Yong); (5/12/21 PM Tr. 90:2-7 (Lander)).

34. The Government relied upon inapplicable studies regarding different enzymes, tissues, and/or incubation times to argue the SVF Surgical Procedure materially changed the SVF Cells. (5/7/21 PM Tr. 27:15-28:9 (Yong; agreeing that different enzymes have different effects on tissues or cells); 5/7/21 PM Tr. 45:7-46:2; 49:4-18; 50:20-51:14; 51:15-52:13 (Yong; testifying that studies she relied upon did not evaluate effect of Liberase on adipose tissue)). The Government relied upon studies focusing on the effect of:

- Collagenase (most similar to Defendant's Liberase) and dispase on spleen cells using a longer incubation time. (5/7/21 PM Tr. 32:17-22; 33:25-34:2; 34:15-18 (Yong)). The collagenase had no effect on the cell surface markers, and in some cases increased the surface markers. (5/7/21 PM Tr. 35:7-24 (Yong)).
- Tumor Dissociation Enzyme on human ovarian tissue. (5/7/21 PM Tr. 39:16-24 (Yong)). Further identifying that Liberase, such as the CSN-TMAX, is "highly purified and formulated for

efficient, gentle and reproducible dissociation of tissues from a wide variety of sources" (5/7/21 PM Tr. 41:10-22 (Yong)).

- Dispase and central nervous system tissue. (5/7/21 PM Tr. 47:11-23 (Yong)).
- Collagenase and muscle stem cells. (5/7/21 PM Tr. 48:16-49:3 (Yong)).
- Mechanical separation and umbilical cord tissue. (5/7/21 PM Tr. 49:19-50:13 (Yong)).

35. None of the articles relied upon by the Government evaluated the effect of Liberase on adipose tissue or SVF Cells. (5/7/21 PM Tr. 52:14-17 (Yong)).

36. Indeed, Dr. Yong did not know which enzyme the SVF Surgical Procedure utilized. (5/7/21 PM Tr. 72:16-23 (Yong)).

37. The FDA has never tested a sample of the Liberase utilized during the SVF Surgical Procedure. (5/7/21 PM Tr. 17-22:2 (Yong)).

38. There is no evidence that the temporary change in shape changes the biological characteristics of the SVF Cells. (5/7/21 PM Tr. 44:21-45:5 (Yong); 5/12/21 AM Tr. 97:7-98:15 (Reid)).

39. The centrifuge does not create any new material during the SVF Surgical Procedure. (5/12/21 PM Tr. 77:21-22 (Lander)).

40. The dextrose lactated ringers solution does not create any new material during the SVF Surgical Procedure. (5/12/21 PM Tr. 78:9-11 (Lander)).

41. The incubator (Celltibator) does not create any new material during the SVF Surgical Procedure. (5/12/21 PM Tr. 80:11-13 (Lander)).

42. There is no new material created by the use of saline during the SVF Surgical Procedure. (5/12/21 AM Tr. 56:20-22 (Berman); 5/12/21 AM Tr. 99:15-23 (Reid)).

43. The Government did not provide evidence or credible testimony to rebut Drs. Berman, Lander, and Reid's evidence and testimony that the SVF Cells that are returned to the patient during the SVF Surgical Procedure are the same SVF Cells that were removed during the SVF Surgical Procedure. [3]

II. THERE IS NO EVIDENCE THAT THE SVF SURGICAL PROCEDURE IS AN ADULTERATED DRUG

44. The SVF Surgical Procedure does not create any new material or introduce any foreign article into the body. (5/12/21 AM Tr. 56:4-6 (Berman); 5/12/21 PM Tr. 46:10-12 (Lander)). Unlike manufactured drugs, the SVF Surgical Procedure does not create any cellular or tissue-based product that did not previously exist within the patient. (5/7/21 PM Tr. 28:18-31:8 (Yong); 5/11/21 AM Tr. 112:20-24 (Berman); 5/12/21 AM Tr. 56:1-3 (Berman)).

A. There Is No Evidence That The SVF Cells Are Held For Sale After Traveling In Interstate Commerce

45. Drs. Berman and Lander do not charge for the SVF Cells. (5/11/21 PM Tr. 50:15-25 (Berman)).

46. Drs. Berman and Lander only charge a surgical fee for the SVF Surgical Procedure. (5/11/21 PM Tr. 50:15-25 (Berman); 5/12/21 AM Tr. 21:1-22:7 (Berman)).

[3] Sitting as fact-finder, the trial court judge is tasked with weighing and making factual findings as to the credibility of witnesses. *Earp v. Davis*, 881 F.3d 1135, 1145 (9th Cir. 2018) (citing *Anderson v. City of Bessemer City, N.C.*, 470 U.S. 564, 575 (1985)) (affirming district court's determination of witness credibility); *Miller v. Thane Int'l, Inc.*, 615 F.3d 1095, 1104 (9th Cir. 2010) (same). Indeed, when findings are based on trial court determinations regarding the credibility of witnesses, even greater deference is given to the court's findings, "for only the trial judge can be aware of the variations in demeanor and tone of voice that bear so heavily on the listener's understanding of and belief in what is said." *Trent v. Valley Elec. Ass'n, Inc.*, 195 F.3d 534, 538 (9th Cir. 1999) (citing *Anderson*, 470 U.S. at 575).

47. Drs. Berman and Lander have provided the SVF Surgical Procedure free of charge to hundreds of patients who wished to undergo the SVF Surgical Procedure but were unable to pay. (5/12/21 AM Tr. 59:16-24 (Berman)).

48. The SVF Cells are extracted and isolated from a patient in California. The SVF Cells are then returned to that patient in California. (5/11/21 PM Tr. 57:1-10 (Berman)).

49. The SVF Cells are not shipped in interstate commerce after they are isolated. (5/11/21 PM Tr. 57:1-10 (Berman)).

50. The Government offered testimony that certain fluids used in the SVF Surgical Procedure cross state lines, but that standard would make every surgical procedure a matter of interstate commerce, which would be contrary to the recognition that surgeries are the practice of medicine and exclusively regulated by State governments. (5/5/21 AM Tr. 11:25-12:8 (Lagud); 5/5/21 PM Tr. 24:11-15 (Forster); 5/5/21 PM Tr. 53:18-24 (Christopher); 5/6/21 AM Tr. 75:23-24 (Lapteva); 5/11/21 AM Tr. 47:14-19 (Jim)).

B. The SVF Surgical Procedure Complies With All California Regulations Regarding Surgical Procedures

51. Drs. Berman and Lander are board certified surgeons. (Ex. 300; 5/11/21 AM Tr. 95:10-15 (Berman); (5/12/21 PM Tr. 51:19-52:21 (Lander)). Drs. Berman and Lander and their practices are regulated by the State of California Medical Board. (5/11/21 AM Tr. 98:8-18 (Berman); 5/12/21 PM Tr. 54:25-55:4 (Lander)). Dr. Berman's facility in Beverly Hills is accredited by the Accreditation Association for Ambulatory Health Care ("AAAHC") per California law. (Ex. 302; 5/11/21 AM Tr. 98:23-100:10 (Berman)).[4]

[4] Dr. Lander's Rancho Mirage facility is not an outpatient surgical center; therefore, the California Medical Board's accreditation requirements do not apply. (5/12/21 PM Tr. 55:23-56:17 (Lander)). Further, accreditation is not required for the SVF Surgical Procedures because only local anesthesia is used. (5/12/21 AM Tr. 63:25-64:6 (Berman)).

52. The operating rooms in which Drs. Berman and Lander perform the SVF Surgical Procedure comply with all health and safety standards established by the California State Medical Board for outpatient procedures. (Exs. 302-322, 5/11/21 AM Tr. 98:8-18 (Berman); 5/12/21 PM Tr. 54:25-55:4 (Lander)).

53. Surgical environments can never be absolutely closed or acceptably closed to the extent required of actual drug manufacturing. (5/11/21 AM Tr. 21:9-16 (Berman)). The SVF Surgical Procedure is a virtually closed procedure with the exception of slight exposure to the operating room air through the aperture of a syringe. (5/11/21 AM Tr. 21:9-16 (Berman)).

III. THERE IS NO EVIDENCE THAT THE SVF SURGICAL PROCEDURE IS A MISBRANDED DRUG

A. The SVF Surgical Procedure Has Adequate Directions For Use

54. Only licensed medical doctors, such as Drs. Berman and Lander, can perform the SVF Surgical Procedure. (ECF No. 113-1, Stipulated Fact No. 4; Ex. 430; 5/11/21 PM Tr. 59:4-13 (Berman)). The Cell Surgical Network ("CSN") affiliates—all licensed physicians who are approved and trained in the investigational studies—agree to follow the SVF Surgical Procedure protocols. (Ex. 431; 5/11/21 PM Tr. 60:6-16 (Berman)).[5]

55. Drs. Berman and Lander have drafted multiple surgical and physician user manuals regarding how to safely perform the SVF Surgical Procedure, including contraindications, sterilization techniques, and detailed step-by-step instructions on how to extract, isolate, and re-implant the SVF Cells. (*See, e.g.*, Exs. 303-322).

56. Drs. Berman and Lander drafted the surgical manual and physician user manual based on their combined 70 years of surgical experience and have

[5] For the reasons stated in II.A., the SVF Cells are not held for sale after traveling in interstate commerce and the FDCA does not apply.

continuously updated the manuals to include techniques developed during the thousands of SVF Surgical Procedure that Drs. Berman and Lander and their affiliated physicians have performed. (Exs. 304, 305; 5/11/21 PM Tr. 17:21-20:13 (Berman)).

57. These surgical manuals were provided to physicians with the CSN-Time Machine® centrifuge and CSN-Time Machine® incubator. The surgical manuals are intended to provide step-by-step instructions so that physicians would have "uniform ability to follow a particular treatment" protocol, involving the same procedure and deployment methods. (5/11/21 PM Tr. 18:10-14; 19:6-12 (Berman)).

58. Physicians can request additional information regarding how to perform the SVF Surgical Procedure, including attending a demonstration of the entire process. (5/11/21 PM Tr. 58:6-59:3 (Berman)).

B. <u>The Isolated SVF Cells Are Labeled Pursuant To Surgical Protocols</u>

59. The SVF Cells isolated during the SVF Surgical Procedure are not placed in any container for preservation, storage, or later use. (5/11/21 PM Tr. 57:1-10 (Berman)). The SVF Cells are transferred between sterile syringes during three washing phases. After the third washing phase, the SVF Cells are re-implanted in the same patient through direct injection or intravenously. (5/11/21 PM Tr. 13:2-9 (Berman)).

60. The syringes containing the SVF Cells are labeled with the patient's name, date, and the description "SVF" pursuant to well-defined surgical patient identifier protocols. (5/11/21 PM Tr. 13:6-9 (Berman)).

IV. THERE IS NO EVIDENCE THAT THE EXPANDED MSC SURGICAL PROCEDURE IS AN ADULTERATED DRUG AND/OR IS MISBRANDED

A. Defendants Perform A Simple Liposuction In Connection With The Expanded MSC Surgical Procedure; They Are Not Manufacturing An Adulterated Drug

61. In addition to the SVF Surgical Procedure, Drs. Berman and Lander perform a procedure whereby a patient's adipose tissue is removed and sent to a GMP-compliant tissue bank to isolate MSC Cells. The MSC Cells are then replicated and stored until the same patients requests that they be returned for implantation into her body (the "Expanded MSC Surgical Procedure"). (5/11/21 PM Tr. 66:10-67:22 (Berman)).

62. During the Expanded MSC Surgical Procedure, a qualified candidate undergoes liposuction at either Dr. Berman or Dr. Lander's medical facilities. (5/11/21 PM Tr. 66:10-19 (Berman)). Drs. Berman and Lander do not perform the remainder of the SVF Surgical Procedure on the harvested adipose tissue but send the tissue to a GMP-compliant third party. (5/11/21 PM Tr. 66:20-68:1 (Berman)).

63. A patient is eligible for the Expanded MSC Surgical Procedure where the individual has a medical condition that will require multiple treatments, but the individual is unable or unwilling to undergo multiple liposuctions. (5/11/21 PM Tr. 64:9-65:1 (Berman))

64. Drs. Berman and Lander do not adulterate, manufacture, process or store the patient's adipose tissue during the Expanded MSC Surgical Procedure. (5/11/21 PM Tr. 66:20-67:22 (Berman)).

65. The third party isolates the MSC Cells from the adipose tissue using a technique that is similar to the SVF Surgical Procedure stated above under GMP laboratory conditions. (5/11/21 PM Tr. 66:20-67:22 (Berman); 5/13/21 PM Tr. 31:20-32:11 (Lander)).

66. The third party then places the MSC Cells in a culture, in which the MSC Cells naturally begin to replicate (*i.e.*, expand in number), thereby creating a sufficient number of cells under GMP conditions for multiple treatments (the "Expanded MSC Cells"). (5/11/21 PM Tr. 66:20-67:22 (Berman)). Replication or propagation is a natural state for stem cells and the Expanded MSC Cells retain all of the biological characteristics of the MSC Cells. (5/13/21 PM Tr. 30:24-31:7 (Lander)).

67. The Expanded MSC Cells retain their cell markers, and do not differentiate while in the culture or during storage. However, the Expanded MSC Cells retain their ability to differentiate into osteoblasts, adipocytes, bone, cartilage, and muscle cells once they are deployed back into the patient. (5/13/21 PM Tr. 31:1-15 (Lander)).

68. The third party tissue bank places the Expanded MSC Cells into a sterile vial labeled with the patient's name, date, and description pursuant to well-defined patient identifier protocols. (5/11/21 PM Tr. 13:6-9 (Berman)).

69. After receiving the Expanded MSC Cells from the third party in a labeled sterile vial, Drs. Berman and Lander deploy the Expanded MSC Cells into the original patient. (5/12/21 AM Tr. 64:23-65:2 (Berman)).

70. Drs. Berman and Lander only utilize GMP facilities to isolate and duplicate the MSC Cells, there is no evidence that MSC Cells are adulterated. (5/13/21 PM Tr. 33:18-23 (Lander); *see also* 5/5/21 AM Tr. 35:22-36:4 (Lagud); 5/5/21 PM Tr. 37:4-19, 38:5-9 (Forster, no deviations from GMP regulations); 5/5/21 PM Tr. 65:25-66:7 (Christopher); 5/11/21 AM Tr. 69:16-25 (Jim)).

71. At the time of the inspection in 2017, Drs. Berman and Lander were sending the adipose tissue to American Cyrostem ("ACS") for isolation of the MSC Cells and storage of the same. (5/4/21 AM Tr. 89:19-90:4 (Lagud); 5/11/21 PM Tr. 66:20-67:22 (Berman)).

72. Drs. Berman and Lander believed that ACS was a GMP facility based on ACS's representations. (5/11/21 PM Tr. 67:23-68:1 (Berman); 5/13/21 PM Tr. 32:12-17 (Lander)). Drs. Berman and Lander ceased utilizing ACS in connection with the Expanded MSC Surgical Procedure following notice from the FDA that ACS was not complying with GMP regulations. (Ex. 90; 5/11/21 PM Tr. 69:3-12 (Berman)).

73. The third party that Drs. Berman and Lander currently use is registered with the FDA and has been inspected by the FDA, with no resulting deficiency letters. This demonstrates that the FDA has found the facility compliant with GMP regulations. (5/12/21 AM Tr. 65:3-14 (Berman)).

74. Any conduct relating to Dr. Berman sending material to ACS was outside of the scope of the 2017 FDA investigation. (5/5/21 PM Tr. 36:10-37:5 (Forster). The FDA did not document any deficiencies relating to the Expanded MSC Surgical Procedure. (5/5/21 PM Tr. 36:1-9 (Forster)). The FDA did not document any deficiencies relating to the receipt of Expanded MSC Cells as part of the inspection. (5/5/21 PM Tr. 37:6-19 (Forster)).

75. The FDA inspected ACS as part of the coordinated inspection of Defendants' facilities. (5/5/21 AM Tr. 6:11-22 (Lagud); 5/5/21 PM Tr. 34:7-10 (Forster); 5/5/21 PM Tr. 59:11-16 (Christopher); 5/11/21 AM Tr. 69:7-12 (Jim)).

76. The FDA issued Form 483 observations to ACS after the inspection, which detailed deficiencies in ACS's facility. (5/5/21 PM Tr. 35:15-25 (Forster)). The FDA issued a warning letter to ACS on January 3, 2018 ("Warning Letter"). (Ex. 90).

77. Yet, in September 2020, the FDA allowed an Investigational New Drug ("IND") Phase 1 Clinical Trial to move forward for ACS's ATCell™ Expanded Autologous, Adipose-Derived Mesenchymal Stem Cells Deployed via Intravenous Infusion for the Treatment of Post-Concussion Syndrome (PCS) in Retired Military and Athletes. (Ex. 500). In March 2021, ACS announced that it

"has begun processing patient's adipose tissue and expanding mesenchymal stem cells (ATCell™) for use in its FDA approved IND Phase I Clinical Trial." (Ex. 501).

78. Drs. Berman and Lander are permitted to perform the SVF treatments on their patients subject to the conditions set forth in the IND approvals for ACS. (5/4/21 AM Tr. 74:21-75:2 (Joneckis)).

79. The Government did not present any evidence that Defendants are adulterating any material in connection with the Expanded MSC Surgical Procedure.

B. <u>There Is No Evidence That The Expanded MSC Surgical Procedure Is Misbranded Or That Drs. Berman And Lander Receive A Misbranded Drug Through The Expanded MSC Surgical Procedure</u>

80. Only licensed practitioners, such as Drs. Berman and Lander or the CSN affiliates can perform the Expanded MSC Surgical Procedure. (ECF No. 113-1, Stipulated Fact No. 4; Ex. 430; 5/11/21 PM Tr. 59:4-13 (Berman)).

81. Drs. Berman and Lander have drafted multiple surgical and user manuals regarding how to safely perform the liposuction procedure, including contraindications, sterilization techniques, and detailed step-by-step instructions on how to harvest the adipose tissue. (Exs. 304, 305; 5/11/21 PM Tr. 17:21-20:13 (Berman)).

82. At all times, the vials containing the Expanded MSC Cells are labeled with the patient's name, date, and description pursuant to patient identifier protocols. (Exs. 304; 305).

83. The Government did not present any evidence that Defendants label or mislabel any material regulated by the FDA in connection with the Expanded MSC Surgical Procedure.

84. The Government did not present any evidence regarding the labeling Defendants receive from any GMP facility in connection with the Expanded MSC Surgical Procedure, nor any evidence that any such labeling is deficient.

C. The Expanded MSC Cells Are Not Held For Sale

85. Drs. Berman and Lander do not charge for the Expanded MSC Cells; they only charge a surgical fee for the liposuction procedure. (5/12/21 AM Tr. 21:1-22:7 (Berman)).

86. Patients paid a separate facility fee to the third party for the banking or storage of the Expanded MSC Cells. (5/12/21 AM Tr. 21:1-22:7 (Berman)).

V. THERE IS NO EVIDENCE THAT THE SVF/ACAM2000 SURGICAL PROCEDURE CAN BE PERFORMED BY DEFENDANTS NOW OR IN THE FUTURE OR THAT IT FALLS UNDER FDA AUTHORITY

A. Defendants Used The SVF/ACAM2000 Surgical Procedure Only As Part Of An Institutional Review Board–Approved Research Study

87. Drs. Berman and Lander partnered with StemImmune, led by Dr. Aladar Szalay, a pioneer in oncolytic virology studies, to study the safety of utilizing SVF Cells as a mechanism to deliver ACAM2000, an oncolytic virus, to the cancer cells ("SVF/ACAM2000 Surgical Procedure"). (Ex. 48; 5/12/21 PM Tr. 96:13-97:15 (Lander)).

88. The SVF/ACAM2000 Surgical Procedure was a limited experimental treatment only available to individuals with terminal cancer for whom traditional treatment had failed. (5/11/21 PM Tr. 71:14-72:4 (Berman)). Drs. Berman and Lander would prepare the SVF Cells using their standard method, then add the ACAM2000 to the SVF Cells ACAM2000 ("SVF/ACAM2000 Cells), before deploying into the same patient's body. (Ex. 48).

89. ACAM2000 is an FDA-approved vaccine. (Ex. 189). There is no evidence that the ACAM2000 utilized in the SVF/ACAM2000 Surgical Procedure was adulterated.

90. ACAM2000 is an oncolytic virus, meaning that it has the ability to kill cancer cells. (5/11/21 PM Tr. 70:11-14 (Berman); 5/12/21 PM Tr. 96:11-18 (Lander)).

91. The federal government maintains exclusive control over ACAM2000 as part of the country's Strategic National Stockpile and it may only be distributed by specific government agencies. (Ex. 380; 5/12/21 PM Tr. 102:19-25, 103:10-15 (Lander)). It is not publicly available, but researchers may request vials for studies. (Ex. 380).

92. Drs. Berman and Lander cannot perform the SVF/ACAM2000 Surgical Procedure without access to ACAM2000. (5/11/21 PM Tr. 73:6-9 (Berman); 5/12/21 PM Tr. 103:10-15 (Lander)).

93. StemImmune was inspected in July 2017 as part of the same overall investigation of Defendants' facilities. (Ex. 503; 5/5/21 PM Tr. 13:7-15 (Forster); 5/5/21 PM Tr. 57:10-16 (Christopher)).

94. The FDA confiscated vials of ACAM2000 from StemImmune's laboratories at the University of California, San Diego in August 2017. (Ex. 383; (5/4/21 PM Tr. 61:4-10 (Lagud); 5/5/21 PM Tr. 30:1-16 (Forster); 5/5/21 PM Tr. 57:6-8(Christopher)).

95. Dr. Berman last performed the SVF/ACAM2000 Surgical Procedure before the FDA's July 2017 inspection. (5/11/21 PM Tr. 72:20-73:5 (Berman)).

96. Dr. Lander last performed the SVF/ACAM2000 Surgical Procedure in June 2016. (5/12/21 PM Tr. 103:7-9 (Lander)).

97. Drs. Berman and Lander have no desire or intention to perform the SVF/ACAM2000 Surgical Procedure outside of proper FDA regulatory approval or a determination that that SVF/ACAM2000 Cells are not a drug and do not fall

under FDCA regulations. (5/11/21 PM Tr. 73:10-13 (Berman); 5/12/21 PM Tr. 103:21-24 (Lander)).

B. The SVF/ACAM2000 Surgical Procedure Is Not Sold And Does Not Implicate Interstate Commerce

98. Drs. Berman and Lander did not charge study participants for the SVF/ACAM2000 Surgical Procedure. (5/11/21 AM Tr. 85:15-18 (Jim); 5/11/21 PM Tr. 72:5-8 (Berman); 5/12/21 PM Tr. 99:4-6 (Lander)).

99. Indeed, Drs. Berman and Lander paid for independent laboratory and radiology fees for study participants. (5/11/21 PM Tr. 72:8-11 (Berman); 5/12/21 PM Tr. 99:7-15 (Lander)).

100. The entire SVF/ACAM2000 Surgical Procedure occurred in California. (Ex. 48; 5/11/21 PM Tr. 57:1-10 (Berman)).

101. The Government did not present any evidence that the SVF/ACAM2000 Cells were shipped in interstate commerce.

C. There Is No Evidence That The SVF/ACAM2000 Surgical Procedure Is Misbranded

102. The SVF/ACAM2000 Cells were not placed in any container for preservation, storage, or later use. (*See* 5/11/21 PM Tr. 57:1-10 (Berman)). They were used as part of the same surgical procedure. (5/11/21 PM Tr. 13:6-9 (Berman)). The syringes containing the SVF/ACAM2000 Cells were labeled with the patient's name and date pursuant to well-defined patient identifier protocols. (5/11/21 PM Tr. 13:6-9 (Berman).

103. The SVF/ACAM2000 Surgical Procedure was performed at all times by Drs. Berman and Lander, licensed physicians. (5/11/21 PM Tr. 70:4-72:18 (Berman)). Drs. Berman and Lander performed the SVF/ACAM2000 Surgical Procedure pursuant to the IRB-approved study protocols, which included detailed step-by-step instructions on how to extract and isolate the SVF Cells, reconstitute the ACAM2000 vaccine, and implant the SVF/ACAM2000 Cells. (Ex. 48).

VI. LACK OF ADEQUATE NOTICE

104. In 2010, Drs. Berman and Lander began developing the SVF Surgical Procedure as part of their surgical practices and as a cutting-edge surgical procedure designed to address their patients' medical concerns. (5/11/21 AM Tr. 109:13-111:6 (Berman); 5/12/21 PM Tr. 57:21-58:8 (Lander)).

105. Drs. Berman and Lander worked with an interdisciplinary team to develop the SVF Surgical Procedure, initially focusing on orthopedic cases. (5/11/21 AM Tr. 107:2-15 (Berman); 5/12/21 PM Tr. 59:7-15 (Lander)). Dr. Berman took the equipment utilized for a fat transfer procedure and refined the equipment to create a nearly closed surgical procedure. (5/11/21 AM Tr. 110:6-18 (Berman)).

106. Drs. Berman and Lander have successfully performed point of care investigative deployment of autologous adipose SVF Cells since 2010 and through CSN since 2012. (5/11/21 PM Tr. 46:8-11 (Berman)).

107. Further, the FDA's 2017 Guidance states that, for some health care providers, the FDA will not allege any violation for three years. Food & Drug Admin., *Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use; Guidance for Industry and Food and Drug Administration Staff* at 9-10 (Nov. 2017 and corrected Dec. 2017) [hereinafter "Food & Drug Admin., *Regulatory Considerations*"]. However, the FDA did not identify to whom the three-year grace period applies. By filing this lawsuit, the FDA singled out Drs. Berman and Lander yet declined to address medical procedures that involve significantly more manipulation of the HCT/Ps. (*Compare id.*, *with* ECF No. 1).

108. The FDA inspected the two CSCTC facilities in July 2017, before the Guidance was finalized. (Exs. 11, 12). The FDA provided written notices of inspection, to which Drs. Berman and Lander responded. (Exs. 38, 39, 69, 70).

The FDA provided no further notice to Drs. Berman and Lander before filing this lawsuit. (*See* Exs. 38, 39, 69, 70; ECF No. 1).

109. During the same time and as part of a coordinated investigation, the FDA inspected ACS (5/5/21 AM Tr. 6:11-22 (Lagud); 5/5/21 PM Tr. 34:7-10 (Forster); 5/5/21 PM Tr. 59:11-16 (Christopher); 5/11/21 AM Tr. 69:7-12 (Jim)) and StemImmune (Ex. 503; 5/5/21 PM Tr. 13:7-15 (Forster); 5/5/21 PM Tr. 57:10-16 (Christopher)).

110. Instead of providing an opportunity to meet and discuss the findings, the FDA filed the complaint in May 2018, well before the three-year grace period expired. (ECF No. 1).

111. The Government does not purport to regulate substantially similar practices. For example, the FDA allows the use of certain stem cells extracted from bone marrow, while attempting to shut Defendant down, even though the cells are essentially identical to the cells found in adipose tissue. (5/12/21 PM Tr. 83:7-9 (Lander)).

112. Similarly, in certain abdominal surgeries, called anastomosis, a segment of the bowel is removed and two pieces are sewed together, then a portion of the omentum (a fat-like sheet covering the intestines) is removed and used to cover the anastomosis to prevent leaks and help heal the bowel. (5/12/21 PM Tr. 86:17-88:14 (Lander)).

113. As another example, neurosurgeons isolate autologous fat from around the patient's umbilical area, crush that fat with a "Spence Cranioplastic roller" to transform it into a thin foil on a separate table in the operating room, and return that "foil" to the patient during the same procedure to repair, not cushion the brain's lining. (5/12/21 PM Tr. 87:22-88:13 (Lander)). This process involves far more processing of the tissue than the SVF Surgical Procedure, and yet is exempted from FDA regulation, appropriately recognized as the practice of medicine. (5/12/21 PM Tr. 87:22-88:13 (Lander)).

CONCLUSIONS OF LAW

I. CLAIMS ONE AND TWO: THE SVF SURGICAL PROCEDURE IS EXEMPT FROM FDA REGULATION AND ALSO IS NOT A DRUG, NOR IS IT ADULTERATED OR MISBRANDED

1. For Claim One, the Government must prove: (1) that the SVF Surgical Procedure involves a drug, (2) that the SVF Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) that the methods used in, or the facilities or controls used for, the manufacture of the drug are not in conformity with current Good Manufacturing Practices ("cGMP"). 21 U.S.C. §§ 331(k), 352(a)(2)(B).

2. For Claim Two, the Government must prove: (1) that the SVF Surgical Procedure involves a drug, (2) that the SVF Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) that it does not contain adequate directions for use or the symbol "Rx." 21 U.S.C. §§ 352(f), 352(b)(2).

3. "You are not required to comply with the requirements of this part if you are an establishment that removes HCT/P's from an individual and implants such HCT/P's into the same individual during the same surgical procedure," 21 C.F.R. § 1271.15(b) (the "SSP Exception").

4. The SSP Exception is a complete defense to Claims Ones and Two and Defendants have established that the SSP Exception applies to the SVF Surgical Procedure.

5. Additionally and alternatively, the Government failed to carry its burden because the SVF Surgical Procedure is not a drug, does not travel through interstate commerce, meets surgical sterility requirements, and is accompanied by adequate directions for use.

A. The SSP Exception Applies To The SVF Surgical Procedure And Operates As A Complete Defense To Any Alleged Noncompliance With FDA Regulations

6. The only legitimate dispute regarding application of the SSP Exception is whether the SVF Cells implanted into the patient are "such HCT/Ps" as were removed from that patient. The answer is unequivocally yes.

7. In evaluating whether the SVF Surgical Procedure satisfies the requirements of the SSP Exception, the appropriate focus is on the SVF Cells. The SSP Exception unambiguously states that the focus is on the target of the removal—either the cell or the tissue—rather than the largest system removed. This is the only permissible interpretation of the SSP Exception, which explicitly includes both "tissues" and/or "cells," through its use of the term "HCT/Ps." *See* 21 C.F.R. §§ 1271.3(d); 1271.15(b). Cells can only be removed from a patient along with larger systems, such as the tissues or organs that they comprise. Focusing on the "tissue" removed while ignoring the target "cells" would eliminate the word "cells" from HCT/Ps and violate the canons of statutory construction.[6]

8. The SVF Surgical Procedure is autologous because it involves collecting a patient's cell population naturally occurring in the patient's adipose tissue and relocating that cell population back into the same patient.

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[6] After the trial on this matter, the Court of Appeals for the Eleventh Circuit issued a decision upholding summary judgment in *United States v. US Stem Cell Clinic, LLC*, No. 19-13276, 2021 WL 2213288 (11th Cir. June 2, 2021). This decision is non-precedential and not binding on this Court. Further, this decision is based on a motion for summary judgment, rather than the full factual record developed in this case. The Eleventh Circuit held that both adipose tissue and SVF Cells are HCT/Ps. *Id.* at *5. Despite this, the Eleventh Circuit agreed with the FDA's position that the relevant HCT/P is the adipose tissue, not the SVF, which has been rejected by this Court. *Compare id.* at *6, *with* Order Deny Mot. Summ. J. (ECF No. 84). As the Government conceded during trial in this case, there is no surgical procedure or other method to remove only the target cells, thus the FDA's reading, adopted by the Eleventh Circuit, fails to give full effect to all words in the SSP Exception. Further, the Eleventh Circuit did not consider or determine if the SVF Cells were the same SVF Cells that were removed. For all these reasons, this Court declines to defer to the Eleventh Circuit's decision.

9. The SVF Surgical Procedure is a single outpatient procedure.

10. Drs. Berman and Lander "remove[] HCT/Ps from an individual and implant[] such HCT/Ps " (*i.e.*, SVF Cells). *See* 21 C.F.R. § 1271.15(b).

11. The SSP Exception does not have any requirement that the HCT/Ps be unaltered before reinsertion into the patient. *See* 21 C.F.R. § 1271.15(b). Any reference to whether the HCT/Ps are manipulated and/or altered are located in a different regulation 21 C.F.R. § 1271.10 (discussing "minimal manipulation"). Defendants do not seek nor need to meet the requirements of 21 C.F.R. § 1271.10, which would result in FDA regulation, albeit in a more limited fashion. To the contrary, Defendants' compliance with the SSP Exception is a complete exemption from all FDA regulation. While the Government argues the application of 21 C.F.R. § 1271.10, the regulation is entirely inapplicable and the two tests should not be conflated. Therefore, there is no requirement that the cells be "minimally manipulated."[7]

12. Regardless, the SVF Surgical Procedure does not alter the biological characteristics of the SVF Cells and those cells remain "such HCT/P" that were removed from the patient. There is no evidence that the cells are anything other than autologous cells removed from, belonging to, and returned back to the patient.

13. Drs. Berman and Lander specifically studied the effect of Liberase on the SVF Cells, found that they have not been altered in any substantive way to change them from their naturally occurring state (*i.e.*, they have the same DNA, same cell type, same flow cytometry markers). (5/12/21 PM Tr. 88:18-89:8 (Lander)). The GMP-grade Liberase does not affect ability of the SVF Cells to differentiate, the cell surface marker expression was similar, and cell viability was not significantly different.

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[7] Even the Eleventh Circuit found it was a mistake for the FDA to conflate the SSP Exception and the minimal manipulation exception. *US Stem Cell Clinic*, 2021 WL 2213288 at *7 n.2.

14. Dr. Lola Reid testified that, based on her more than forty-five years of experience studying stem cells, the Liberase used to separate the SVF Cells does not break down, damage, or in any way alter the phenotypic traits and biological properties of the SVF Cells. The Liberase, as used in the SVF Surgical Procedure, has no impact on the viability of the SVF Cells, yield of cells, and, most significantly, has no effect on the phenotype (identifying cell markers), the ability of the cells to differentiate, to proliferate, or to function in their intended capacity.

15. Dr. Reid testified that the Liberase does not penetrate the stem cells or destroy the surface of the stem cells, it solely enzymatically digests the extracellular matrix.

16. Dr. Reid further testified that the SVF Cells are not altered at any point during the SVF Surgical Procedure. The SVF Cells are not chemically altered. There are no genes added to or removed from the SVF Cells. The genetic makeup of the cells do not change.

17. Finally, Dr. Reid testified that the biological and functional characteristics of the SVF Cells do not change, including ability to proliferate. The re-implanted SVF Cells retain all their functional abilities, such as regenerative tissue repair and healing and anti-inflammatory properties.

18. The Government did not take samples of or test the SVF Cells or Liberase, despite the ability to do so. The Government did not present any evidence regarding the effect of Liberase on SVF Cells. As such, any Government claim regarding the effect of Liberase or the SVF Cells lacks foundation and credibility.

19. The Court finds that Dr. Berman and Dr. Lander are well qualified to opine and testify on the practice of medicine, development of surgical procedures, the SVF Surgical Procedure, and the effect of Liberase on the SVF Cells. The Court finds Defendants' evidence and testimony more credible than Dr. Yong given her failure to analyze the appropriate enzyme, and particularly, her testimony

that she did not know which enzyme Drs. Berman and Lander use. Further, Defendants have actually tested the product at issue (as published in a peer-reviewed journal), while the Government has never collected a sample or tested the SVF Cells or Liberase despite the ability to do so.

20. In conclusion, the SSP Exception applies to the SVF Surgical Procedure and is a complete defense to Claims One and Two.[8]

21. Because the SSP Exception applies to the SVF Surgical Procedure, Defendants do not fall under FDA jurisdiction, are not governed by the FDCA or associated regulations; therefore, the Government is not entitled to injunctive relief against Defendants.

1. The FDA's Interpretation Of The SSP Exception Is Not Entitled To Deference Because The Exception Is Unambiguous

22. The SSP Exception is unambiguous, thus there is no need for deference to the FDA's interpretation. *See Kisor v. Wilkie*, 139 S. Ct. 2400, 2414 (2019) ("[T]he possibility of deference can arise only if a regulation is genuinely ambiguous."); *Christensen v. Harris Cnty.*, 529 US 576, 588 (2000) ("The regulation in this case, however, is not ambiguous . . . . To defer to the agency's position would be to permit the agency, under the guise of interpreting a regulation, to create *de facto* a new regulation.").

23. Here, the FDA, under the guise of interpretation, is attempting to substantively change, and thereby create, a new regulation that the HCT/Ps must remain in their "original form." This language does not appear anywhere in the

[8] The Government completely ignores 21 C.F.R. part 1271, which states that biological drugs are governed by Current Good Tissue Manufacturing Practice (cGTMP) and not the general Current Good Manufacturing Practice (cGMP) regulations. *See* 21 C.F.R. § 1271.20 ("If my HCT/P's do not meet the criteria in 1271.10, and I do not qualify for any of the exceptions in 1271.15, what regulations apply?"). The Government provided no evidence of failure to comply with cGTMP but focused entirely on the broader and inapplicable cGMP regulations.

SSP Exception. The Supreme Court has repeatedly rebuked such efforts. *See Azar v. Allina Health Serv.*, 139 S. Ct. 1804, 1810-11 (2019) (requiring substantive regulatory changes to comply with APA notice and comment requirements and requirements to meet with stakeholders). The adoption of the 2017 Guidance is not a valid modification of the existing regulation because it was not subject to a proper notice and comment period and was not signed by a United States Senate-confirmed officer.

24. HCT/Ps are defined as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient." 21 C.F.R. § 1271.15(b). The regulation is not ambiguous. Under the explicit terms of the regulations, the SVF Surgical Procedure falls within the exception because the SVF Cells are removed and implanted in the same surgical procedure. The FDA's recent interpretation that seeks to create ambiguity is not entitled to deference.

2. The FDA's Interpretation Of The SSP Exception Is Unreasonable

25. The FDA's interpretation of the SSP Exception is unreasonable and creates enforcement inconsistency: it makes no logical sense to assert that the SSP Exception applies to a procedure where physical cutting is necessary to isolate needed tissue but not where chemical "cutting" is necessary to isolate needed cells—especially given the use of both "cells" and "tissue" in the SSP Exception. *See Kisor*, 139 S. Ct. at 2415–16 ("[T]he agency's reading must fall within the bounds of reasonable interpretation . . . a requirement an agency can fail.").

26. A characterization that focuses on the target of the removal is more reasonable than one that includes everything that was removed. Undoubtedly, most if not all surgical removals take out more biological matter than what was targeted. Take, for example, the removal of an artery for implantation back in the body. *See* U.S. Dep't Health & Human Services, Food & Drug Admin., *Same*

Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception (Nov. 2017) ("SSP Exception Guidance Document") ("Examples [of procedures considered same surgical procedures] include autologous skin grafting, and coronary artery bypass surgery involving autologous vein or artery grafting."). Along with the needed artery, a surgeon may remove some blood. She may also remove more artery tissue than what will ultimately be needed. Similarly, surgeons isolate autologous fat from around the patient's umbilical area, crush that fat with a "Spence Cranioplastic roller" to transform it into a thin foil on a separate table in the operating room, and return that "foil" to the patient during the same procedure to repair, not cushion the brain's lining. If a piece of muscle and its overlying fascia (connective tissue) were removed in order to provide a fascial graft to repair large tissue defects, the muscle (tissue) would no longer have its ability to repair, reconstruct or replace, but the "tissue product" (*i.e.* the fascia) would still retain its biological characteristics and could be utilized. But again, the surgeon is not required to implant everything that was removed.

27. The SSP Exception does not require that the surgeon implant everything that was removed—including the removed blood and excess artery—for it to apply. The SSP Exception Guidance expressly recognizes that processing steps such as "rinsing [and] cleansing" or "sizing and shaping," including "dilation," "cutting," "meshing," of HCT/Ps do not take a procedure out of the SSP Exception. *See* Food & Drug Admin., *Regulatory Considerations*.

28. The logic that not all that is removed must be implanted applies to the SVF Surgical Procedure as well. The SSP Exception undoubtedly applies to a procedure that removed only SVF Cells and then implanted only those same SVF Cells back into the patient. But that technology did not and still does not yet exist. Accordingly, Drs. Berman and Lander must remove SVF Cells as part of a larger biological system. And like the surgeon who washes the blood from the artery and

cuts it down to the right size, Drs. Berman and Lander use an enzyme and a centrifuge to isolate the targeted HCT/Ps from the unneeded biological material that was also removed.

29. The FDA's unreasonable interpretation is not entitled to deference.

3. The FDA's Interpretation Should Not Be Considered Because It Constitutes Unfair Surprise

30. The FDA's interpretation of "such HCT/Ps" under the 2017 Guidance pronounces an entirely new position regarding the applicability of the SSP Exception, and directly contradicts twenty years of FDA pronouncements on the issue, resulting in "unfair surprise" to Drs. Berman and Lander and others providing autologous SVF surgical therapies. *See Kisor*, 139 S. Ct. at 2418 ("And a court may not defer to a new interpretation, whether or not introduced in litigation, that creates 'unfair surprise' to regulated parties."); 21 C.F.R. § 1271.15(b) (2001) (adopting regulatory scheme initially proposed in 1997).

31. Further, the FDA informed the public, including Drs. Berman and Lander, that they would have a three-year grace period (until December 2020) to determine how best to regulate procedures involving HCT/Ps. *See* Food & Drug Admin., *Regulatory Considerations* at 21. The FDA did not wait for that three-year period to end for Drs. Berman and Lander, even though Drs. Berman and Lander are one of the few organizations that had actually been working with the FDA on an Investigational Device Exemption (Ex. 323) through the Center for Biological Evaluation and Research for the overarching surgical system, as each individual medical device was already FDA-cleared.

32. The FDA's interpretation constitutes unfair surprise and is not entitled to deference.

B. Even If The SSP Exception Did Not Apply, The SVF Surgical Procedure Is Not A Drug And Is Not Introduced Into Interstate Commerce

1. The FDA Lacks Authority To Regulate Physicians Performing Surgery, Instead This Is Exclusively Within A State's Jurisdiction

33. Pursuant to the FDCA, the FDA has the authority to regulate drugs introduced into interstate commerce (21 U.S.C. § 321), and pursuant to the Public Health Service Act (42 U.S.C. § 201), the authority to regulate biological products introduced into interstate commerce. "Drugs" are defined as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man." However, this definition is irrelevant to the Court's analysis because a surgical procedure is also intended for the "diagnosis, cure, mitigation, treatment, or prevention of disease in man."

34. Congress explicitly rejected any attempt to "limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship." 21 U.S.C. § 396. Indeed, Congress recognized the limitations of the FDA and rejected "any intent to directly regulate the practice of medicine." *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 351 n.5 (2001) (citing Beck & Azari, FDA, Off–Label Use, and Informed Consent: Debunking Myths and Misconceptions, 53 Food & Drug L.J. 71, 72 (1998) (stating that "[o]ff-label use is widespread in the medical community and often is essential to giving patients optimal medical care, both of which medical ethics, FDA, and most courts recognize")); *U.S. ex rel. Modglin v. DJO Glob. Inc.*, 114 F. Supp. 3d 993, 999 (C.D. Cal. 2015), *aff'd sub nom. United States v. DJO Glob., Inc.*, 678 F. App'x 594 (9th Cir. 2017).

35. Drs. Berman and Lander are physicians, practicing medicine and performing surgery using FDA-cleared medical devices and FDA-approved prescription pharmaceuticals through their medical practices California Stem Cell Treatment Center ("CSCTC") and CSN. Title 21 of the United States Code section 360 exempts "practitioners licensed by law to prescribe or administer drugs or devices and who manufacture, prepare, propagate, compound, or process drugs or devices solely for use in the course of their professional practice" from registering with the FDA. Section 360 recognizes that the FDA does not have authority over a licensed physician practicing medicine entirely within the State of California using FDA-approved and FDA-cleared pharmaceuticals and devices. The FDA cannot modify this law via regulation, particularly not in a manner that violates notice and comment procedure and the Appointments Clause (U.S. Const. Article II, § 2, cl. 2). And, as courts have recognized, the FDA generally does not regulate doctors—particularly those using office-based drugs or biologicals for the sole use of their patients. *Buckman*, 531 U.S. at 350; *see also Houston v. Medtronic, Inc.*, No. 2:13-cv-01679-SVW (SHx), 2014 WL 1364455, *1 n.1 (C.D. Cal. April 2, 2014) ("Physicians are permitted to use Class III devices in off-label manners"); *U.S., ex rel. Modglin*, 114 F. Supp. 3d at 999; *Amarin Pharma, Inc. v. FDA*, 119 F. Supp. 3d 196, 200 (S.D.N.Y. 2015). Thus, at a minimum, Drs. Berman and Lander's actions are exempt from regulation and/or protected by statute as lawful "off-label" uses of FDA-approved drugs and medical devices.

36. Indeed, allowing the FDA to expand its regulatory authority to encompass Drs. Berman and Lander's surgical procedures would allow the FDA to regulate not only an individual's private relationship with her physician, but also the individual's use of her body and medical decisions. *See Roe v. Wade*, 410 U.S. 113 (1973). These activities implicate fundamental rights of privacy and bodily autonomy. *See Griswold v. Connecticut*, 381 U.S. 479, 485 (1965). Thus, to hold that the FDA can regulate the SVF Surgical Procedure as if the SVF Cells were a

saleable commodity ignores the fundamental and constitutional differences between drugs and an individual's right to control her body and the cells that comprise it.

37. Drs. Berman and Lander can use FDA-cleared medical devices and FDA-approved pharmaceuticals in any manner that they determine is best to care for and treat their patients. While SVF Cells are not a drug for the reasons stated above, and even if they were, each step of the SVF Surgical Procedure uses FDA-cleared and/or approved medical devices and pharmaceuticals. *See* 21 U.S.C. § 396.

38. Drs. Berman and Lander are practicing medicine, not creating pharmaceuticals.

2. The Government Has No Authority Over Defendants Because The SVF Surgical Procedure Does Not Involve The Sale Of Cells And Does Not Implicate Interstate Commerce

39. The SVF Cells used in each procedure are not fungible goods and cannot be sold or patented—Defendants do not sell the SVF Cells. *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 579 (2013) (holding that naturally-occurring human body parts that are a "product of nature and not patent eligible merely because it has been isolated."). As the cells cannot be patented, the cells cannot be owned by anyone other than the patient from whom they were removed, nor could they be "sold back" to the patient.

40. Finally, the uniqueness of the SVF Cells used in each surgical procedure present further constitutional implications. The Government is seeking to regulate not only an individual's private relationship with her physician, but also the individual's use of her body and medical decisions. These are not a "'class of activities' that have a substantial effect on interstate commerce." *Gonzales v. Raich*, 545 U.S. 1, 17 (2005). Rather, these are activities that implicate fundamental rights of privacy and bodily autonomy. *See Griswold*, 381 U.S. at

485. This Court rejects the Government's invitation to regulate the SVF Surgical Procedure and its related procedures as if the SVF Cells were any other commodity, which ignores the fundamental and constitutional difference between drugs shipped in interstate commerce and an individual's right to control his/her own body and the cells therein.

41. Indisputably, the SVF Cells are not shipped or introduced into in interstate commerce because the entire procedure takes place in California.

42. This Court rejects the Government's attempt to extend federal regulations to an article that does not affect interstate commerce, as required by the Commerce Clause, U.S. Const. art. I, § 8, cl. 3, and that is not introduced or shipped in interstate commerce, as defined by the FDCA, 21 U.S.C. § 321(b).

43. Because the SVF Cells are not shipped or sold in interstate commerce, the Government's claims against Defendants not only exceed the scope of the Commerce Clause, but they also exceed the FDA's statutory authority.[9] *See 62 Cases, More or Less, Each Containing Six Jars of Jam v. United States*, 340 U.S. 593, 600 (1951) ("In our anxiety to effectuate the congressional purpose of protecting the public, we must take care not to extend the scope of the statute beyond the point where Congress indicated it would stop."); *see Panama Ref. Co. v. Ryan*, 293 U.S. 388, 430 (1935) ("[T]here are limits of delegation which there is no constitutional authority to transcend."). Section 331(k) prohibits "any . . . act with respect to a food, drug, device, tobacco product, or cosmetic, if such act is done while such article is held for sale (whether or not the first sale) ***after shipment in interstate commerce*** and results in such article being adulterated or

[9] Each of the FDA Investigators recognized this constitutional and statutory limitation on FDA authority: the mere use during surgery of a product that traveled through interstate commerce is not sufficient to create FDA jurisdiction. Accordingly, the use of common surgical crystalloid fluids, including saline and dextrose lactated ringers solution, during the SVF Surgical Procedure does not give rise to FDA jurisdiction. (5/5/21 AM Tr. 11:25-12:8 (Lagud); 5/5/21 PM Tr. 24:11-15 (Forster); 5/5/21 PM Tr. 53:18-24 (Christopher); 5/11/21 AM Tr. 47:14-19 (Jim)).

misbranded." 21 U.S.C. § 331(k) (emphasis added). The FDCA defines "interstate commerce," as "(1) commerce between any State or Territory and any place outside thereof, and (2) commerce within the District of Columbia or within any other Territory not organized with a legislative body." 21 U.S.C. § 321(b). Because the article must be ***introduced or shipped*** in interstate commerce, rather than merely affect interstate commerce, the scope of the FDCA does not reach the full extent of the Commerce Clause.

C. There Is No Adulteration Because Defendants Meet All California Regulations Governing Surgical Facilities

1. California Law Governs The Safety Of Surgical Facilities

44. Drs. Berman and Lander have continually complied with California law governing their medical practices. California law provides that "[n]o association, corporation, firm, partnership, or person shall operate, manage, conduct, or maintain an outpatient setting in this state, unless the setting is []: . . . [a]n outpatient setting accredited by an accreditation agency approved by the division pursuant to this chapter." Cal. Health & Safety Code § 1248.1(g). Further, the Medical Board of California has set standards for accreditation, which each accreditation agency must adopt to ensure the health and safety of outpatient procedures. *Id.* at § 1248.15(a). These requirements relate to (1) proper licensing of health staff, (2) facility safety and emergency training requirements, (3) maintenance of clinical records, (4) a system for patient care and monitoring procedures, and (5) quality assessment and improvement. *Id.* The accreditation agency must inspect the facility as often as necessary and no less often than once every three years. *Id.* at § 1248.35.

45. Defendants have complied with California law governing health and safety requirements of medical facilities. Defendants met all requirements governing patient rights and responsibilities; governance; administration; quality of care; quality management and improvement; maintenance of clinical records and

health information; infection prevention, control, and safety; general safety; facilities and environment, anesthesia services; surgical and related services; and pharmaceutical services.

46. The FDA introduced no evidence that Defendants do not comply with California law governing medical facilities.

2. The SVF Surgical Procedure Does Not Manufacture Drugs

47. Unlike traditionally manufactured pharmaceutical drugs, SVF Cells—like the BRCA1 and BRCA2 genes at issue in *Ass'n for Molecular Pathology*, 569 U.S. 576—cannot be patented because they are naturally occurring human body parts that are a "product of nature and not patent eligible merely because it has been isolated." *Id.* at 579. Thus, applying a regulatory regime crafted to oversee the pharmaceutical drug industry to naturally occurring autologous stem cells simply makes no practical sense; especially where the SVF Cells are the sole property of the patient and could never be sold.

48. Defendants perform the SVF Surgical Procedure for the benefit of their patients; therefore, they are not drug manufacturers and fall outside of the purview of the FDA. *See* 21 U.S.C. §§ 360, 396.

D. There Is No Misbranding Because Each Procedure Is Completed By A Trained Physician And Defendants Provide Adequate Directions For Use

49. Labels on prescription drugs and devices provide the physician, a learned intermediary, with all of the information that the physician needs to make an informed decision regarding course of conduct. *See, e.g.*, *T.H. v. Novartis Pharm. Corp.*, 4 Cal. 5th 145, 164 (2017) ("In the context of prescription drugs, a manufacturer's duty is to warn physicians about the risks known or reasonably known to the manufacturer . . . . If the manufacturer provides an adequate warning to the prescribing physician, the manufacturer need not communicate a warning directly to the patient who uses the drug."); *Motus v. Pfizer Inc.*, 196 F. Supp. 2d

984, 990-91 (C.D. Cal. 2001) *aff'd sub nom.* 358 F.3d 659 (9th Cir. 2004) ("California follows the learned intermediary doctrine").

50. Defendants provide surgical manuals, user manuals, and the detailed IRB-approved deployment protocols with the CSN-Time Machine® centrifuge and CSN-Time Machine® incubator. *See* 21 U.S.C. § 321(m) (defining "labeling" as any material accompanying a drug or device). Additionally, physicians can request additional information regarding how to perform the SVF Surgical Procedure or Expanded MSC Surgical Procedure including attending a demonstration of the entire procedure. These manuals and instructions provide physicians with all information that she needs to make an informed decision regarding course of conduct for her patient.

51. The information contained within the surgical manuals, user manuals, and deployment protocols are based upon clinical proof as shown by the numerous articles demonstrating both effectiveness and safety of the SVF Surgical Procedure.

52. Defendants' clinical studies have continuously operated under an IRB protocol and review. *Contra United States v. Cole*, 84 F. Supp. 3d 1159, 1169 (D. Or. 2015) (granting summary judgment where the defendants "conducted no controlled studies and collected no clinical data"). The IRB is independent from Drs. Lander and Berman, and they do not and have never served in any capacity on the ICSS IRB.

53. Additionally, the Government's allegation that there should be an "Rx" symbol is irrational. The procedures do not require any prescription labeling because they are surgical procedures. The SVF Cells are not placed in any container for preservation, storage, or later use. The SVF Cells are transferred between sterile syringes during three washing phases. After the third washing phase, the SVF Cells are placed in syringes labeled with the patient's name, date, and the description "SVF" pursuant to well-defined patient identifier protocols.

Immediately thereafter, the SVF Cells are re-implanted in the patient through direct injection or intravenously.

II. CLAIMS THREE, FOUR, AND FIVE: THE GOVERNMENT FAILED TO SHOW THAT DEFENDANTS MANUFACTURE A DRUG OR THAT DEFENDANTS RECEIVE A MISBRANDED DRUG

54. For Claim Three, the Government must prove: (1) that the Expanded MSC Surgical Procedure involves a drug, (2) that the Expanded MSC Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) that the methods used in, or the facilities or controls used for, the manufacture of the drug are not in conformity with current Good Manufacturing Practices ("cGMP"). 21 U.S.C. §§ 331(k), 352(a)(2)(B).

55. For Claim Four, the Government must prove: (1) that the Expanded MSC Surgical Procedure involves a drug, (2) that the Expanded MSC Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) that it does not contain adequate directions for use of the symbol "Rx." 21 U.S.C. §§ 352(f), 352(b)(2).

56. For Claim Five, the Government must prove: (1) that the Expanded MSC Surgical Procedure involves a drug, (2) that the Expanded MSC Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) Defendants received a misbranded drug for pay or otherwise.

57. First, the Government failed to carry its burden that Defendants do any processing that would be considered adulteration. Second, the Government failed to carry its burden that Defendants misbranded any product or that the labeling received was inadequate. Third, there is no interstate commerce because the patient does not pay for Expanded MSC Cells but only for the Expanded MSC Surgical Procedure.

A. The Government Failed To Carry Its Burden That Defendants Process Or Manufacture Expanded MSC Cells

58. The Government must concede that Defendants do not process the adipose tissue as part of the Expanded MSC Surgical Procedure. During Drs. Berman and Lander's Expanded MSC Surgical Procedure, a qualified candidate undergoes liposuction at either Dr. Berman or Dr. Lander's medical facilities. There can be no doubt that this is the practice of medicine. Indeed, an FDA Investigator admitted that any conduct relating to Defendants sending adipose tissue to ACS (a third party tissue bank) was outside of the scope of the investigation.

59. Drs. Berman and Lander do not perform the remainder of the SVF Surgical Procedure on the harvested adipose tissue but send the tissue to a GMP-compliant third party in a sterile transport container.

60. The evidence established that Defendants always intended to, and the Expanded MSC Cells are currently, isolated in an FDA-registered, GMP-compliant tissue bank.

61. Drs. Berman and Lander currently use a tissue bank in Florida, which is registered with the FDA, has undergone GMP compliance inspections, and has not received any Form 483 Observations, meaning that the FDA has found the tissue bank to be GMP-compliant.

62. The Government failed to establish any adulteration of the Expanded MSC Cells by Defendants. Instead, each of the Government Investigators confirmed that there was no evidence that the Expanded MSC Cells were adulterated.

63. As a matter of law, the Government cannot prove that Defendants are manufacturing, much less adulterating the Expanded MSC Cells, thus there is no

FDA jurisdiction. (*See* 5/5/21 PM Tr. 19:6-15 (Forster, admitting no jurisdiction if no manufacturing occurring); *id.* at 57:23-59:7 (Christopher, same)).[10]

B. The Government Failed To Carry Its Burden That Defendants Misbrand Expanded MSC Cells

64. Again, the Government concedes that Defendants do not label the Expanded MSC Cells—a third party tissue bank does. Drs. Berman and Lander solely perform the liposuction surgical procedure, then ship the adipose to the third party GMP facility in a sterile transport container. No labeling of Expanded MSC Cells occurs in Defendants' medical facilities.

65. The Government failed to establish any misbranding of the Expanded MSC Cells by Defendants. Instead, the evidence showed that Defendants sent the adipose tissue to the third-party facility for further processing and labeling.

66. As a matter of law, the Government cannot prove that Defendants misbranded the Expanded MSC Cells because Defendants did not create any such labels.

C. The Government Failed to Carry Its Burden That Defendants Received Misbranded Expanded MSC Cells, Regardless 21 U.S.C. § 360 Permits Receipt Of Propagated Products

1. The Government Failed To Provide Any Evidence Of The Labeling Received From The Third Party Tissue Banks

67. The Government did not introduce any evidence regarding the labeling associated with the Expanded MSC Cells received from the GMP third party. Nor did the Government introduce any evidence regarding the current

[10] *United States v. Regenerative Scis., LLC*, 741 F.3d 1314 (D.C. Cir. 2014), is not applicable because the Government sued the facility where the MSC Cells were isolated and expanded. Here, the Government did not sue ACS; therefore, the purported manufacturer is not a party to this litigation. Defendants cannot be enjoined for the actions of an non-party.

labeling. Any argument that the Expanded MSC Cells were misbranded is entirely speculative.

68. The FDA Investigators did not collect samples of the labeling. The FDA Investigator admitted that the receipt of materials from ACS was within her investigation, and she did not find any deviations in GMP (which includes labeling requirement (*see* 21 C.F.R. § 1271.250). (5/5/21 PM Tr. 37:4-19 (Forster)). There is no evidence regarding the labeling accompanying any Expanded MSC Cells upon receipt by Defendants.

69. The Government argues that because of the nature of the Expanded MSC Cells, there is no labeling that would be sufficient for physicians to make an informed decision. However, given the FDA's recent IND approval of ACS's Expanded MSC Cells, the ATCell™ Product, which would have considered safety data and proposed protocols relating to appropriate use, the FDA must have determined that the safety data and protocols support proceeding to human use. (5/7/21 AM Tr. 41:10-42:10 (Lapteva)).

2. Defendants Are Permitted To Use Any Propagated Product For The Care Of Their Patients

70. When Defendants receive the Expanded MSC Cells from the GMP tissue bank, Defendants may use those cells in connection with the treatment and care of their patients without separately having to register with the FDA. *See* 21 U.S.C. § 360.

71. Each of the tissue banks that Defendants have used or currently use are registered with the FDA. Defendants are expressly exempted from registering with the FDA if they are manufacturing, preparing, propagating, compounding, or processing drugs solely for the use of their patients. 21 U.S.C. § 360. It is undisputed that Defendants receive Expanded MSC Cells solely for the use of their patients and the Government has not provided any evidence to demonstrate

otherwise. Accordingly, Defendant do not need to independently register with the FDA or otherwise comply with FDA regulations to receive propagated products.

72. Further, because there is an existing IND for ACS's Expanded MSC Cells, Drs. Berman and Lander are permitted to use Expanded MSC Cells for the care and treatment of their patients without falling under FDA jurisdiction. *See* 21 U.S.C. §§ 360, 396. Defendants are permitted to use the FDA-approved IND protocols in an off-label purpose to care for their patients. *See* 21 U.S.C. § 396; *see also Houston*, 2014 WL 1364455, *1 n.1; Right to Try Act of 2017, Pub. L. No. 115-176 (codified at 21 U.S.C. § 360-bbb-0a).

73. The Government has not established that Defendants receive a misbranded drug. Regardless, Congress has expressly exempted Defendants, as physicians, from FDA statutes and regulations regarding receipt of propagated products.

D. <u>The Expanded MSC Cells Are Not Sold In Interstate Commerce</u>

74. The patients are not paying for Expanded MSC Cells (nor could they pay for their own cells) but are instead paying Drs. Berman and Lander for the surgical procedure, including a mini liposuction. Further, there is no interstate commerce as the Expanded MSC Cells are not fungible goods and cannot be patented or sold. *See Ass'n for Molecular Pathology*, 569 U.S. at 579 (holding that naturally-occurring human body parts that are a "product of nature and not patent eligible merely because it has been isolated."); *Gonzales*, 545 U.S. at 17 (2005).

75. Again, the Expanded MSC Surgical Procedure is a personal decision between a physician and her patient. The Government is overreaching and seeking to implicate fundamental rights of privacy and bodily autonomy by controlling a patient's access to medical care. *See Griswold*, 381 U.S. at 485. This is well beyond the FDA's authority.

III. CLAIMS SIX AND SEVEN: THE GOVERNMENT LACKS STANDING TO ENJOIN THE SVF/ACAM2000 SURGICAL PROCEDURE, AND IT CONSTITUTES PERMISSIBLE OFF-LABEL USE

76. For Claim Six, the Government must prove: that (1) the SVF/ACAM2000 Surgical Procedure involves a drug, (2) the SVF/ACAM2000 Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) the methods used in, or the facilities or controls used for, the manufacture of the drug are not in conformity with current Good Manufacturing Practices ("cGMP"). 21 U.S.C. §§ 331(k), 352(a)(2)(B).

77. For Claim Seven, the Government must prove: (1) that the SVF/ACAM2000 Surgical Procedure involves a drug, (2) that the SVF/ACAM2000 Surgical Procedure involves a drug that is held for sale in interstate commerce; and (3) that it does not contain adequate directions for use of the symbol "Rx." 21 U.S.C. §§ 352(f), 352(b)(2).

78. The Government fails to prove that it has standing for injunctive relief.

79. Additionally and alternatively, Defendants used an FDA-approved medication in a permissible off-label manner as part of a clinical research study. The patients did not pay for any of the treatment and it was never available to the general public.

1. The Government Lacks Standing To Seek Injunctive Relief For The SVF/ACAM2000 Surgical Procedure

80. Article III standing requires a present case or controversy, and it is well-settled that "[p]ast exposure to illegal conduct does not in itself show a present case or controversy regarding injunctive relief . . . ." *Lujan v. Defenders of*

Wildlife, 504 US 555, 564 (1992).[11] The Ninth Circuit has explained that to satisfy the standing requirements under *Lujan*, a plaintiff seeking prospective injunctive relief "must demonstrate that he has suffered or is threatened with a concrete and particularized legal harm, coupled with a sufficient likelihood that he will again be wronged in a similar way." *Bates v. United Parcel Serv., Inc.*, 511 F.3d 974, 985 (9th Cir. 2007) (citations and quotations omitted); *see also Chapman v. Pier 1 Imports (U.S.) Inc.*, 631 F.3d 939, 946 (9th Cir. 2007) (en banc) (citations and quotations omitted) (holding a plaintiff "must demonstrate a real and immediate threat of repeated injury in the future" for Article III injunctive relief standing). The party asserting the claim has the burden of establishing these elements. *Chandler v. State Farm Mut. Auto. Ins. Co.*, 598 F.3d 1115, 1122 (9th Cir. 2010). A plaintiff must demonstrate standing separately for each form of relief sought. *Los Angeles v. Lyons*, 461 U.S. 95, 109 (1983) (notwithstanding the fact that plaintiff had standing to pursue damages, he lacked standing to pursue injunctive relief).

81. The Government has not met its burden of establishing standing to pursue injunctive relief regarding the SVF/ACAM2000 Surgical Procedure because Drs. Berman and Lander stopped performing the procedure by June 2017, well before the initiation of this lawsuit and before the seizure of the ACAM2000.

82. Defendants cannot perform the SVF/ACAM2000 Surgical Procedure without the ACAM2000, which is in the exclusive control of the Government and otherwise inaccessible to Defendants.

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[11] Defendants acknowledge that the Government has Article III standing under *Lujan* and does not need to establish the general requirements for standing to bring an action. *See Consumer Fin. Protection Bureau v. Gordon*, 819 F.3d 1179, 1187. However, the Government is still required to make a showing that it has standing to pursue injunctive relief, *i.e.*, that there is a showing that the defendants' conduct is likely to recur. *Id.* at 1197-98.

83. The Government has no evidence of Drs. Berman and Lander's medical practices or SVF/ACAM2000 Surgical Procedure since July 2017.

84. Drs. Berman and Lander have no desire or intention of performing the SVF/ACAM2000 Surgical Procedure absent formal regulatory approval or confirmation that the SVF/ACAM2000 Surgical Procedure is not governed by the FDCA, but rather is the practice of medicine.

2. Defendants Are Permitted To Compound Products For The Care Of Their Patients

85. Defendants are expressly exempted from registering with the FDA if they are compounding, *i.e.*, combining, solely for the use of their patients. 21 U.S.C. § 360. Here, it is undisputed that ACAM2000 is an FDA-approved vaccine. Defendants are permitted to compound ACAM2000 with the patient's SVF Cells as a matter of law.

86. Drs. Berman and Lander exclusively used the SVF/ACAM2000 Surgical Procedure for the benefit of their patients; therefore, they are not drug manufacturers and fall outside of the purview of the FDA. *See* 21 U.S.C. § 360.

87. Drs. Berman and Lander used ACAM2000 for an off-label purpose, which is explicitly permitted under the FDCA. 21 U.S.C. § 396. Physicians may utilize any FDA-approved drug for an off-label purpose that they determine is the best course of treatment for their patients. *Houston*, 2014 WL 1364455, *1 n.1 *Modglin*, 114 F. Supp. 3d at 999. Thus, Drs. Berman and Lander's actions were protected as lawful "off-label" uses of FDA-approved drugs and medical devices.

3. The SVF/ACAM2000 Surgical Procedure Was Not Sold In Interstate Commerce And Did Not Travel Through Interstate Commerce

88. First, the study participants did not pay for the SVF/ACAM2000 Surgical Procedure. Second, the compounded SVF/ACAM2000 Cells were not held for sale after shipment in interstate commerce and the isolation of the SVF

Cells and combination with ACAM2000 all occured within California. *See* 21 U.S.C. § 331(k) (prohibiting act "***after shipment in interstate commerce***[, which] results in such article being adulterated or misbranded" (emphasis added)).

89. There was no interstate commerce as the SVF/ACAM2000 Cells were not fungible goods and could not be patented or sold. *See Ass'n for Molecular Pathology*, 569 U.S. at 579 (holding that naturally-occurring human body parts that are a "product of nature and not patent eligible merely because it has been isolated."); *Gonzales*, 545 U.S. at 17.

90. Again, the Expanded SVF/ACAM2000 Surgical Procedure was a personal decision between a physician and her patient and is protected from Government overreach into bodily autonomy. *See Griswold*, 381 U.S. at 485. This is well beyond the FDA's authority.

IV. THE GOVERNMENT HAS ARBITRARILY ENFORCED THE SSP EXCEPTION, AND DEPRIVED DEFENDANTS OF APPROPRIATE NOTICE

91. The Government's actions depriving Drs. Berman and Lander of their property are arbitrary and capricious and fail to provide adequate due process. Due process "bar[s] certain [arbitrary wrongful] government actions regardless of the procedures used to implement them." *Daniels v. Williams,* 474 US 327, 331 (1986). An agency's decision to modify regulations must be rational, based on relevant factors and within the scope of the agency's authority. *Motor Veh. Mfrs. Ass'n v. State Farm Ins.,* 463 U.S. 29, 42-43 (1983). An agency cannot create a regulation to nullify existing statutes—21. U.S.C. §§ 360, 396—which explicitly recognize that the practice of medicine is not governed by the FDCA or PHSA. The exacting standards placed on agency decision is required because "the strength of the modern government[] can become a monster which rules with no practical limits on its discretion." *New York v. United States*, 342 U.S. 882, 884 (1951) (dissenting opinion). Finally, where a defendant has modified its behavior based

on the prior statements, the agency's action is subject to closer review. *See Nat. Gas Pipeline Co. of Am. v. Fed. Energy Reg. Comm.*, 590 F2d 664 (7th Cir. 1979) (finding agency acted unreasonably when it substantively modified requirements after the company relied on them and acted to its detriment).

92. As explained above, the nonbinding 2017 Guidance substantively amends 21 C.F.R. § 1271.15 by adding new language (and requirements) to the SSP Exception. The FDA fails to provide any meaningful analysis as to why its longstanding understanding of the SSP Exception required change. The FDA's decision to modify the regulations is irrational.

93. Further, the 2017 Guidance states that, for some health care providers, it will not allege any violation for three years. However, the FDA fails to identify to whom the three-year grace period applies. Instead, the FDA has arbitrarily enforced the new requirement, singling out Drs. Berman and Lander while permitting medical procedures that involve significantly more manipulation of the HCT/Ps. Indeed, the FDA inspected two additional facilities, ACS and StemImmune, at the same time as Defendants and did not file a complaint against either.

94. The Government fails to provide any reasoning for its arbitrary and capricious actions. The FDA's actions cannot stand, especially here where Drs. Berman and Lander relied upon the longstanding regulations to develop a successful new surgical technique and expand their business. An agency decision can be overturned if it is (a) arbitrary and capricious, (b) illegal (fails to follow the APA) or (c) unconstitutional (violating Appointments Clause and property and privacy rights). The FDA's decisions and actions in this case meet all three standards and Drs. Berman and Lander are entitled to attorneys' fees due to wrongful prosecution of invalid regulations.

V. DEFENDANTS ARE ENTITLED TO ATTORNEYS' FEES

95. Congress enacted the Equal Access to Justice Act under 28 U.S.C. § 2412 ("Section 2412") to limit the United States government's immunity to an award for costs and fees. Section 2412 was designed as a gap-filler and applies in the absence of another statute that addresses the issue of attorneys' fees in the case at issue. 28 U.S.C. § 2412(b), (d) ("except as otherwise specifically provided by statute . . ."). Section 2412 is generally applicable whenever the federal government is a party in a civil action. 28 U.S.C. § 2412(d).

96. Given the Government's vast resources and power, Congress determined that parties should be entitled to attorneys' fee where the Government lacks substantial justification for bringing a civil action. Accordingly, Section 2412(d) permits a court to award attorneys' fees and other expenses to a prevailing party unless the Court finds that the Government was "substantially justified." The Supreme Court has concluded that the standard for substantial justification is no different than a "reasonable basis" test. *Pierce v. Underwood*, 487 U.S. 552, 565 (1988). The Court makes one determination regarding the action as a whole, not to each cause of action. *See Ibrahim v. U.S. Dept. of Homeland Sec.,* 835 F.3d 1048, 1054–57 (2016) (holding that court's decision regarding substantial justification requires a "single inquiry focused on the government's conduct in the case as a whole").

97. Here, the Government has acted unreasonably in contravention of well-established regulatory law. First, the SSP Exception applies to the SVF Surgical Procedure on its face. Second, the Government's attempt to rely upon the nonbinding 2017 Guidance violates well-established principles of administrate law and is not substantially justified. Third, the Government has continued to pursue injunctive relief as to the Expanded MSC and SVF/ACAM2000 Surgical Procedures even though Drs. Berman and Lander have (1) ceased using the non-

GMP facility for the Expanded MSC Surgical Procedure, and (2) cannot perform the SVF/ACAM2000 Surgical Procedure due to lack of access to ACAM2000.

98. Accordingly, Drs. Berman and Lander are awarded attorneys' fees because the Government lacked substantial justification for continuing the litigation.

Dated: _____

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HONORABLE JESUS G. BERNAL
United States District Judge

Presented by:

/s/ Celeste M. Brecht
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